DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 09/02/2008 has been entered.

Status of Action

Receipt of Amendments/Remarks filed on 09/02/2008 is acknowledged. Claims 25-62 are pending in this application. Claims 1-24 have been previously cancelled; claims 25, 35 have been previously amended; claims 26-34, 36-54 are previously presented; claims 55-62 have been previously withdrawn.

Receipt of Declarations of 37 CFR 1.131 and 1.132 filed on 09/02/2008 are acknowledged. However, the Declarations have not been considered because they identify a serial number other than the instantly application. The declaration will be considered once the correction is made and resubmitted.

Status of Claims

Accordingly, claims **25-54** are presented for examination on the merits for patentability as they read upon the elected subject matter and claims 55-62 directed to non-elected invention are withdrawn.

Rejections and/or objections not reiterated from the previous Office Action are hereby withdrawn. The following rejection(s) is/are either reiterated or newly applied. They constitute the complete set of rejections and/or objections presently being applied to the instant application.

DOUBLE PATENTING

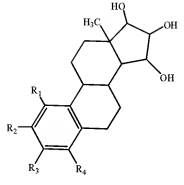
The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 25-32, 45-54 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 20-28, 30, 32-33 of co-pending U.S. Patent Application No. 10/532,320.

Instant claims are drawn to a method of treating or prophylactically treating estrogen-sensitive tumors, i.e. breast cancer, uterine cancer, ovarian cancer, endometriosis, melanoma, benign prostatic hyperplasia, in a mammal by administering a therapeutically effective amount of an estrogenic component to said mammal, wherein the estrogenic component is represented by the formula as below:



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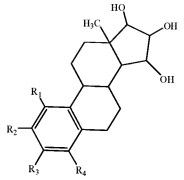
in which formula R_1, R_2, R_3, R_4 independently are a hydrogen atom, a hydroxyl group or an alkoxyl group with 1-5 carbon atoms, or precursor capable of liberating a substance or the estrogenic substance as recited therein.

The conflicting claims are drawn to a method of treating or preventing estrogen-suppressed tumors in a mammal by administering to said mammal a therapeutically effective

amount of an estrogenic component, wherein the estrogenic component is represented by the formula shown below:



;

in which formula R_1, R_2, R_3, R_4 independently are a hydrogen atom, a hydroxyl group or an alkoxyl group with 1-5 carbon atoms, or precursor capable of liberating a substance or the estrogenic substance as recited therein, wherein the estrogen-suppressed tumors can be benign or malign tumors.

The instant and conflicting claims differ in that the instant claims recite the estrogen-sensitive tumors can be breast cancer, uterine cancer, ovarian cancer, endometriosis, melanoma, and benign prostate hyperplasia, whereas the conflicting claims broadly recite the estrogen-suppressed tumors can be benign and malign tumors.

It would have been obvious for one of ordinary skill in the art to utilize the same estrogenic compound as recited in the conflicting claims and try it in the method of treating or prophylactically treating tumors such as breast cancer, uterine cancer, ovarian cancer, endometriosis, melanoma, or benign prostatic hyperplasia because said estrogenic compound is useful for treating or preventing estrogen related benign and malign tumors as suggested in the conflicting claims.

Therefore, one of ordinary skill in the art, at the time the claimed invention was made, would have readily recognized that claims **20-28, 30, 32-33** of the co-pending U.S. Patent Application No. 10/532,320 and claims **25-32, 45-54** of the instant application are obvious variant and are not patentability distinct.

Response to Arguments

Applicants' arguments filed on 09/02/2008 have been fully considered but they are not persuasive.

Applicants argue that the claims in the '320 Application have not been allowed. As such, Applicants are not required to address this provisional rejection at this time, and will address this provisional rejection if and when claims 20-24 in the '320 are allowed (see Remarks: page 2).

Applicants are reminded that the "provisional" double patenting rejection should continue to be made by the Examiner in each application as long as there are conflicting claims in more than one application unless that "provisional" double patenting rejection is the only rejection remaining in one of the applications." See MPEP 822.01.

Claim Rejections - 35 USC § 112 first paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Scope of Enablement of the Invention

Claims 25-44 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Claims 25-44 while being **enabling for "treating"** estrogen-sensitive tumors as claimed comprising administering a therapeutically effective amount of said estrogen compound with an aromatase inhibitor, **does not reasonably provide enablement for "prophylactically treating"** said estrogen-sensitive tumors in the aforementioned method due to the diverse origination and causes of said tumors. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

An analysis of whether the scope of a particular claim(s) is actually supported by the disclosure in a patent application requires a determination of whether the disclosure, at the time of filing, contained sufficient information regarding the subject matter of the claim at issue so as to enable one skilled in the pertained art to use the claimed invention without undue experimentation. *In re Wands*, 8 USPQ 2d 140 (Fed. Cir. 1988). Therefore, the test of enablement is not whether experimentation is necessary, but rather, if experimentation is in fact necessary, whether it is reasonably considered to be undue. *In re Angstadt*, 190 USPQ 214, 219 (CCPA 1976). Determining the issue of enablement with respect to a claim is a question of law based on underlying factual findings. *In re Vaeck*, 20 USPQ 2d, 1444 (Fed. Cir. 1991). More particularly, there are many factors to be considered in determining whether there is sufficient

evidence to support a determination that a disclosure does not satisfy the enablement requirement of 35 U.S.C. § 112, first paragraph, and whether any necessary experimentation is reasonably considered to be "undue". See *In re Wands* at page 1404. MPEP § 2164.01(a). The court in *In re Wands* set forth the following factors to be considered, which included, without limitation, the: 1). scope or breadth of the claims; 2). nature of the invention; 3). relative level of skill possessed by one of ordinary skill in the art; 4). state of, or the amount of knowledge in, the prior art; 5). level or degree of predictability, or a lack thereof, in the art; 6). amount of guidance or direction provided by the inventor; 7). presence or absence of working examples; and 8). quantity of experimentation required to make and use the claimed invention based upon the content of the supporting disclosure. When the above factors are weighed, it is the examiner's position that one skilled in the art could not practice the invention without undue experimentation.

Scope or breadth of the claims:

The claims are broader in scope than the enabling disclosure. The specification merely discloses, without more, the method of prophylactically treating estrogen-sensitive tumors by administering an effective amount of said estrogenic compound with an aromatase inhibitor to a mammal. However, Applicant is purporting that said estrogenic compound co-administered with an aromatase inhibitor in said method can effectively treat estrogen-sensitive tumors in a mammal, or can effectively and prophylactically treat said estrogen-sensitive tumors from occurrence, even though the multitude of these diseases are diversely originated, implicate that all causes and factors that may give rise to said tumors can be treated or prophylactically treated by administering the combination of said estrogenic compound and an aromatase inhibitor.

Nature of the invention:

The nature of the invention is directed to a method of treating or prophylactically treating estrogen-sensitive tumors in a mammal, such as breast cancer, uterine cancer, endometriosis, and recited therein, by administering an effective amount of said estrogenic compound and an aromatase inhibitor to a mammal.

State of, or the amount of knowledge in, the prior art:

It is known in the current state of the art that tumors arise from many different aspects and causes, such as diet, environment or genetics, for examples. Some of these factors are being assessed as risk factors that may increase the chance of developing cancer and some of these factors are being assessed as protective factors that may decrease the chance of developing cancer. Currently, the approach to prophylactically treating cancer is based on the assessment of risk factors and protective factors a person may encounter. However, some risk factors for cancer can be avoided, but some cannot. Likewise, increase the protective factors may only lower the risk of developing a cancer, but does not completely inhibit the occurrence of a cancer (see National Cancer Institute: Breast cancer prevention retrieved online 08/07/2007 from the internet http://www.cancer.gov/templates/doc.aspx?viewed=D972A74B-D25A-4F86-B8ED-33EB3C0450E4&version, page 1). For examples, as of to date, the cause for ovarian cancer is still unknown (see Medline Plus®: Medical Encyclopedia: Ovarian cancer retrieved online on 08/09/2007 from the internet https://www.nlm.nih.gov/medlineplus/ovariancancer.html, page 1 dated on 07/31/2007) or there is still no cure for endometriosis (see National Institute of Child Health and Human development, NIH Publication No. 02-2413 retrieved online on 08/09/2007).

Since prophylactically treating a disease from occurring, one must first know the cause that induces the occurring of such disease. Currently, there is still no known method can prophylactically treating the occurrence of some diseases, such as the estrogen-sensitive tumors, for examples.

Amount of guidance or direction provided by the inventor:

Although the instant specification discloses that the administration of estetrol and tamoxifen (see specification, examples 2-5) for treating mammary tumor; it remains silent on the use of said estrogenic compound with an aromatase inhibitor, as claimed, for the prophylactically treating said estrogenic-sensitive tumors.

Presence or absence of working examples:

The specification provides some scientific data and working embodiments with respect to the administration of estetrol and tamoxifen for treating mammary tumors only (see specification, page 20-27: examples 2-5). However, in the specification, there is no working example or guidance provided for prophylactically treating the occurrence of claimed estrogen-sensitive tumors.

Level or degree of predictability, or a lack thereof, in the art:

A high degree of unpredictability exists in the state of the art regarding how to prophylactically treating tumors formation. Risk factors evaluation, although, may help to avoid the chances of tumor formation; however, at this stage of the art, many of them are still an unsolved puzzle to the scientific field and there is lack of knowledge in the art to inhibit the

occurrence (or prophylactic or prevent) of tumors absolutely due to some uncontrollable genetic risk factors. For example, women who have inherited genetic defect(s) or mutation in the *BRCA1* and *BRCA2* genes may have a higher risk of developing a breast cancer (see Breast Cancer Prevention retrieved online 08/07/2007 from the internet http://www.cancer.gov/cancertopics/pdq/prevention/breast/Patient/page 3) than those who does not inherit such genetic defect(s).

Quantity of experimentation required to make and use the claimed invention based upon the content of the supporting disclosure:

One of ordinary skill in the art would be required to conduct an undue amount of experimentation to reasonably and accurately determine whether said estrogenic compound when co-administering with an aromatase inhibitor in corresponding instant method does in fact effectively and prophylactically treating the occurrence of said estrogenic-sensitive tumors.

Therefore, in conclusion, it is readily apparent from the aforementioned disclosure, in conjunction with a corresponding lack of scientific data and working embodiments, the prophylactically treating estrogen-sensitive tumors is not enabled because the specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Response to Arguments

It is noted to Applicants that claims 25 and 35 are drawn to methods of treating or prophylactically treating estrogen-sensitive tumours and recited therein. The Examiner takes the

position that the term "prophylactically" means the same as "prevention", which is a preventive measure designed and used "to prevent a disease from occurring" (see Prophylactic definition - Medical Dictionary of Popular Medical Terms: retrieved on 03/14/2008 via www.medterms.com/script/main/art.asp?articlekey=11902). Since the term "prophylactic" means the same as "preventive"; therefore, instant claims 25-44 are still construed to be directed to a method of "preventing" estrogen-sensitive tumors in a mammal, and thus, they are rejected for the reason as set forth above.

Claim Rejections - 35 USC § 112 second paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter, which the applicant regards as his invention.

Claim **34** rejected 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 34 recites the limitation "the method, according to claim 25, comprising co-administration of an aromatase inhibitor". There is insufficient antecedent basis for this limitation in the claim because precedent claim 25 does not recite the method comprises an aromatase inhibitor. If Applicants intend to claim an aromatase inhibitor in combination with the recited estrogen compound, the term "further" is required in claim 34 for clarification. It is suggested that the phrase "the method according to claim 25, further comprising..." be adopted.

Conclusion

No claims are allowed.

Contact Information

Any inquiry concerning this communication from the Examiner should direct to Helen Mei-Ping Chui whose telephone number is 571-272-9078. The examiner can normally be reached on Monday-Thursday (7:30 am – 5:00 pm). If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor Johann Richter can be reached on 571-272-0646. The fax phone number for the organization where the application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either PRIVATE PAIR or PUBLIC PAIR. Status information for unpublished applications is available through PRIVATE PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the PRIVATE PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/H.C./

Examiner, Art Unit 1616

/Johann R. Richter/

Supervisory Patent Examiner, Art Unit 1616